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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/084,380	02/28/2002	Daniel G. Chain	20555/1203301-US3	3496

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EXAMINER	
BALLARD, KIMBERLY A	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 03/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/084,380	CHAIN, DANIEL G.	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,19,20,25,51,52,55,56,59,60,63,64 and 71-92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,19,20,25,51,52,55,56,59,60,63,64 and 71-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 January 2006 has been entered.

Applicant has amended claims 14, 20, 51, 52, 55, 56, 59, 60, 63, 64, 71, and 72. Claims 1-13, 15-18, 21-24, 26-50, 53-54, 57-58, 61-62, and 65-70 have been cancelled either previously or in this amendment. New claims 73-92 have been added. Following the amendment, claims **14, 19-20, 25, 51, 52, 55, 56, 59, 60, 63, 64,** and **71-92** are pending and under examination in this office action.

The Examiner of U.S. Patent Application No. 10/084,380 has changed. In order to expedite the correlation of papers with the application, please direct all future correspondence to Examiner Ballard, Technology Center 1600, Art Unit 1649.

Information Disclosure Statement

A signed and initialed copy of the IDS submitted 10 January 2006 is enclosed in this action.

Priority

As noted in the office action of 10 February 2005, Applicant was advised that with regards to the priority date, the effective filing date of the instant application is considered to be the filing date of 28 February 2002.

Claim Objections

Claims 89-92 are objected to because of the following informalities: the claims appear to be substantial duplications of claims 14, 20, 77, and 83, respectively. Unless applicant can provide evidence that the outcome of the recited method of administering the recited antibody (i.e., inhibiting the accumulation of Aβ as in claims 14 and 77, or inhibiting neurotoxicity as in claims 20 and 83) would be substantially different in each case, the claims are considered duplicate claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 19-20, 25, 51-52, 55-56, 59-60, 63-64, 71-92 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *methods for inhibiting accumulation or neurotoxicity of amyloid β peptide in a subject suffering from Alzheimer's disease*, does not reasonably provide enablement for *methods for inhibiting accumulation or neurotoxicity of amyloid β peptide in a subject in need of such*

inhibition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The claims are broadly drawn to methods for inhibiting accumulation or neurotoxicity of amyloid β peptide in the brain, comprising administering to a subject in need of such inhibition a free-end specific antibody targeted to an amyloid β peptide, to inhibit the accumulation or inhibit the neurotoxicity of said amyloid β peptide in said subject. However, the subjects needing inhibition of Aβ accumulation or neurotoxicity recited in these claims encompass a genus of subjects with amyloid-related diseases or conditions.

The instant specification discloses that the invention relates to methods of treating Alzheimer's disease or other diseases characterized by amyloid β deposition, such as mild cognitive impairment (MCI), cerebral amyloid angiopathy or congiophylic angiopathy, Down Syndrome-associated Alzheimer's disease, and inclusion-body myositis. However, the prophetic working example provided in the specification discloses the use of anti-Aβ antibodies for treatment of Aβ-related pathology in a mouse

model of Alzheimer's disease (AD), which would not necessarily be a suitable model for the other diseases disclosed as their etiology differs from AD. No examples, prophetic or otherwise, of the treatment of other amyloid-related diseases are disclosed. The specification is thus lacking in guidance on the treatment of amyloid-related diseases and disorders other than Alzheimer's disease.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims, and the predictability of treatment of diseases and disorders associated with amyloid deposits is quite complex and outside the realm of routine experimentation, because accurate predictions of successful therapies are limited. Since detailed information regarding the treatment of any subject with an amyloid-associated disease are lacking, it is unpredictable as to which subjects having which amyloid-related diseases or disorders, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass any subject needing inhibition of amyloid-β accumulation or neurotoxicity, it would require undue experimentation for one of skill in the art to use the claimed invention in its full scope.

Additionally, the various diseases associated with amyloid deposits recited in the instant specification would each require treatment tailored to their specific disease etiology, and may differ substantially from Alzheimer's disease pathology. For example, a recent review by Buxbaum (*Neurology*, 66(Suppl 1): S110-S113, January 2006) notes that whereas in AD, amyloid deposits form extracellularly, amyloid deposits in inclusion-body myositis are found intracellularly (see abstract). Hence, the claimed methods

using anti-Aβ antibodies for therapy would be impractical for use in treatment of inclusion-body myositis because the antibodies would either not be able to contact the Aβ deposits contained within intracellular vacuoles, or if they could bind intracellular Aβ, they would not be able to subsequently initiate a clearance response.

Due to the large quantity of experimentation necessary to determine the effectiveness of treatment in various subjects, the lack of direction/guidance presented in the specification regarding the same, the complex nature of the invention, the unpredictability of therapy as evidenced in the art, and the breath of the claims which effectively fail to limit a specific patient population, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 14, 16-20, 22-25, 51-52, 55-56, 59-60, and 67-68 under 35 U.S.C. 102(b) in the previous office action dated 9 September 2005 is withdrawn in view of Applicant's arguments and amendments to the claims filed 10 January 2006.

Claims 14, 19-20, 25, 59-60, 63-64, 71-74, 76-77, 80, 82-83, 86, and 88-92, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,786,180 to König et al., issued 7/28/98 (as listed on Applicant's IDS received 1/10/06),

as evidenced by Solomon et al. ("Disaggregation of Alzheimer β-amyloid by site-directed mAb." *PNAS*, April 1997, 94: 4109-4112).

The claims are directed to methods of inhibiting accumulation of or inhibiting the neurotoxicity of amyloid β peptide in the brain of a subject by administering a free-end specific antibody which is targeted to an amyloid β peptide. The instant specification defines "free end specific" as "a molecule which binds specifically to a free terminus/end of an Aβ peptide or to any fragment thereof to slow down or prevent the accumulation of amyloid-β peptides in the extracellular space, interstitial fluid and cerebrospinal fluid and to block the interaction of Aβ peptides with other molecules that contribute to the neurotoxicity of Aβ," ([0062]).

König et al. disclose the therapeutic use of a monoclonal antibody in the prevention of aggregation of amyloid-β peptides, such as amyloid-β depositions in Alzheimer's disease brains (see column 4, lines 57-59 and column 5, lines 57-59). The monoclonal antibody disclosed (for example, mAb 369.2B) is specific for the C-terminal end of Aβ 1-42 (see column 4, lines 3-6). König also discloses that the monoclonal antibody is capable of recognizing derivatives of Aβ 1-42, such as 4-42 species and other truncated forms with the "42" carboxy end, in human body fluids or tissues (see column 7, line 63 – column 8, line 1). The 369.2B mAb, which was raised against Aβ 35-42 (see column 7, lines 45-49), would therefore recognize and bind such truncated amyloid β fragments as Aβ 3-42, Aβ 11-42, or Aβ 17-42 as recited in instant claims 77, 83, and 91-92. König also notes that the disclosed antibody binds to diffuse and fibrillar amyloid, neurofibrillary tangles, and vascular amyloid while being specific for the Aβ

peptide free C-terminal residue 42 (see column 8, lines 18-22), thus meeting recited limitations of instant claims 63, 64, 71-74, 76, 82, and 88.

It is noted that the antibodies of the instant invention have the capacity to *both* inhibit Aβ accumulation *and* inhibit Aβ-related neurotoxicity. Therefore, administration of such an antibody for therapeutic purposes would necessarily result in both of the aforementioned outcomes, namely inhibition of Aβ accumulation and inhibition of Aβ neurotoxicity. For example Solomon et al. reports that specific monoclonal antibodies that were effective in reducing *in vitro* aggregated Aβ (see Figure 1, p. 4110 for example) were also effective in reducing the neurotoxic effects of aggregated Aβ on cultured PC-12 cells (see p. 4111, Discussion and Figures 4 and 5). In other words, neurotoxicity is directly related to the aggregated forms of Aβ, so reducing the accumulation of these aggregated forms would necessarily result in a reduction in neurotoxicity. Therefore, therapeutic administration of the monoclonal anti-Aβ antibody disclosed by König would, in its inhibition of Aβ peptide aggregation, also inhibit Aβ-associated neurotoxicity in a subject, thus meeting recited limitations of instant claims 20, 83, 90, and 92. Thus, the König patent anticipates the instant claims.

Claims 14, 19-20, 25, 51-52, 55-56, 81, 87, and 89-90, as amended, are rejected under 35 U.S.C. 102(b) as being anticipated by Bard et al. "Peripherally administered antibodies against amyloid β-peptide enter the central nervous system and reduce pathology in a mouse model of Alzheimer disease." *Nature Med.*, August 2000, 6(8):

916-919, as evidenced by Su & Ni, *J Neurosci Res*, 1998, 53: 177-186 and Frenkel et al., *J Neuroimmunol*, 1998, 88: 85-90.

The claims are directed to methods of inhibiting accumulation or the neurotoxicity of amyloid β peptide by administration of a free-end specific antibody to a subject in need of such inhibition, wherein the antibody is targeted to the free N-terminus of Aβ peptide. Bard et al. teaches the administration of various monoclonal antibodies to transgenic PDAPP mice, and the reduction of amyloid-β pathologies as a result of this administration (see Abstract). PDAPP mice are used a model of Alzheimer's disease (AD), as the mice over-express human amyloid precursor protein (APP) leading to the accumulation of amyloid-β plaques in the brains of these mice as they age, consistent with AD pathology. Therefore, these transgenic mice qualify as subjects in need of inhibition of Aβ accumulation and/or Aβ-induced neurotoxicity. Bard teaches that the antibodies employed for such treatment include the monoclonal antibodies 3D6 and 10D5. While Bard is silent as to the specific epitopes of these monoclonal antibodies, the epitopes for these antibodies were nonetheless known in the art. For example, Su and Ni recite that the epitope for the 3D6 antibody is Aβ 1-5 (see p. 78, Figure 1) and Frenkel et al. report that the epitope for 10D5 is Aβ 3-6 (see Abstract). Both 3D6 and 10D5 are N-terminal monoclonal antibodies, and, because the epitope for 3D6 is Aβ 1-5, it meets a limitation of instant claims 55-56. Similarly, with the epitope for 10D5 being Aβ 3-6, the antibody would be expected to specifically bind to free N-terminal amyloid-β fragments truncated at position 3, as recited in instant claims 77, 81, 83, 87, and 91-92. Moreover, because the antibodies were shown to effectively reduce amyloid-β burden in

the frontal cortex when administered to PDAPP mice (see p. 917, Figure 1) and initiate both *in vivo* (see p. 917, Figure 2) and *ex vivo* (see p. 918, Table 1) amyloid clearance, they meet the definition of "free-end specific" antibodies recited in the instant claims and *supra*. Also, the 3D6 and 10D5 antibodies would be capable of reducing Aβ-related neurotoxicity in view of their significant amyloid-β clearing effect, as discussed *supra*. Finally, Bard concludes that the monoclonal antibodies are capable of crossing the blood-brain-barrier at therapeutically relevant levels and therefore should be considered for the treatment of Alzheimer's disease as well as other CNS disorders (see p. 919, 1st column). Thus, the Bard et al. reference anticipates instant claims 14, 19-20, 25, 51-52, 55-56, 81, 87, and 89-90.

Claims 14, 19-20, 25, 51-52, 55-56, 59-60, 63-64, 71-77, 80-83, 86-92 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,787,637 to Schenk, issued 7 September 2004, effective filing date 28 November 2000.

Schenk discloses methods of preventing or treating a disease associated with amyloid deposits of Aβ in the brain of a patient, such as Alzheimer's disease, by administering an antibody that binds to induces a clearing response against the amyloid deposits (column 2, lines 22-25 and lines 53-55). The antibody used in such methods can be humanized or chimeric, monoclonal or polyclonal (column 2, lines 59-61), and includes fragments such as separate heavy and light chains, Fab', F(ab')2, Fabc, and Fv (column 7, lines 24-29), and may also be bispecific or bifunctional (column 7, lines 35-39). Schenk teaches that in some methods, the antibody binds to an epitope

comprising a free N-terminal residue of Aβ (column 2 lines 45-46). Examples of such antibodies include the monoclonal antibodies 3D6, whose epitope comprises residues 1-5 of Aβ, and 10D5, with an epitope disclosed as Aβ3-6 (column 14 lines 20-25), thus meeting recited limitations of instant claims 51-52, 55-56, 77, 80-81, 83, 86-87, and 91-92. Schenk discloses that some antibodies bind specifically to the aggregated form of Aβ without binding to the dissociated form (column 13, lines 19-21). Such antibodies are disclosed to bind to naturally occurring short forms of Aβ (i.e. Aβ39, 40 or 41) without binding to a naturally occurring long form of Aβ (i.e., Aβ42 and Aβ43), and some antibodies bind to a long form without binding to a short form (column 13, lines 23-27). Because of this specificity in binding between long and short forms of Aβ, the epitope for these particular antibodies would need to be located in the C-terminus in order to differentiate between the long and short forms of Aβ. Therefore, Schenk discloses C-terminal specific antibodies, thus meeting recited limitations of instant claims 59-60, 63-64, 71-76, 82, and 88. Accordingly, claims 14, 19-20, 25, 51-52, 55-56, 59-60, 63-64, 71-77, 80-83, 86-92 are anticipated by the Schenk patent.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 63-64 and 71-72 under 35 U.S.C. 103 in the previous office action dated 9 September 2005 is withdrawn in view of Applicant's amendments to the claims and in view of Applicant's response filed 10 January 2006.

Claims 78-79 and 84-85 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,787,637 B1 to Schenk, issued 7 September 2004, effective filing date 28 November 2000 in view of Saido et al., *Neurosci Lett*, 1996, 215: 173-176 and Harigaya et al., *Biochem Biophys Res Comm*, 2000, 276: 422-427.

The claims are drawn to methods for inhibiting the accumulation or neurotoxicity of Aβ comprising administering to a subject a free-end specific antibody which is targeted to an amyloid β peptide fragment that begins with a pyroglutamate residue at position 3 (as in claims 78 and 84) or at position 11 (as in claims 79 and 85).

The teachings of Schenk in US 6,787,637 are discussed *supra*. Additionally, Schenk teaches that the principal component of the senile plaques characteristic of Alzheimer's disease is the peptide Aβ (column 1, lines 35-36), and thus methods of reducing such amyloid deposits are disclosed, such as therapeutic antibodies that specifically bind to Aβ or another component of amyloid plaques (column 13, lines 16-17). For example, the therapeutic use of the monoclonal antibodies 10D5 (epitope: Aβ3-6), 266 (epitope: Aβ13-28), and 21F12 (epitope: Aβ33-42), and a polyclonal antibody (raised against Aβ1-42 (AN1792)) in transgenic PDAPP mice to decrease amyloid burden (measured by evaluating Aβ levels in the cortex, hippocampus, and cerebellum) is disclosed (see Example XI). The polyclonal raised against AN1792 was

shown to significantly reduce Aβ levels in the cortex, hippocampus and cerebellum of PDAPP mice (see Tables 13-15 and column 61, lines 33-35). However, while Schenk addresses modifications in immunogenic fragments of Aβ, such as peptides containing unnatural amino acid substitutions (see column 11, lines 23-42), Schenk is silent with respect to antibodies specifically binding these Aβ analogs.

Saido et al. teaches antibodies that bind to truncated forms of Aβ, such as antibodies starting at residues 3 or 11 wherein these glutamate residues have been dehydrated to become pyroglutamate (see p. 174, Figure 1). Specifically, these antibodies are recited as anti-N3(pE) and anti-N11(pE), and bind to the truncated amyloid species of $A\beta_{3(pE)-42}$ and $A\beta_{11(pE)-42}$, respectively (see Figure 1). Saido teaches that these truncated molecules are resistant to major aminopeptidases, and that once produced extracytoplasmically, these species ($A\beta_{N3(pE)-42}$ and $A\beta_{N11(pE)-42}$) would be difficult to catabolize. The resistance of these species to aminopeptidases could therefore reduce Aβ degradation and contribute to deposition (see p. 175, 2nd column).

Harigaya et al. teaches that Aβ peptides with amino-terminal modifications (in particular a species with pyroglutamate at position 3, $A\beta_{N3(pE)-42}$) are found to be deposited in senile plaques of patients with Alzheimer's disease, constituting approximately 25% of the AβX-42(43) that is present (see Abstract and Figure 1, p. 424). It was also shown that the $A\beta_{N3(pE)-42}$ species was also more prone to form oligomers *in vitro* than the unmodified Aβ1-42 species, which Harigaya suggests may contribute to increased aggregation and neurotoxicity when theses species are present (see p. 436, 1st column and Figure 3). Taken together with the Saido reference, this

evidence would implicate an important role for $A\beta_{N3(pE)-42}$ in the pathogenesis of Alzheimer's disease.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to arrive at the claimed invention by incorporating the teachings of Saido and Harigaya on truncated Aβ peptides containing pyroglumate residues ($A\beta_{3(pE)-42}$ and $A\beta_{11(pE)-42}$) and antibodies that bind to them into the methods of treating Alzheimer's as taught by the Schenk in the '637 patent, wherein the artisan would administer antibodies directed against $A\beta_{N3(pE)-42}$ and $A\beta_{N11(pE)-42}$ for treatment. The person of ordinary skill in the art would have been motivated to administer the antibodies taught in Saido therapeutically because Harigaya teaches that the $A\beta_{N3(pE)-42}$ truncated peptides are found at a high percentage in the senile plaques of patients with Alzheimer's disease, and therefore these peptides may significantly contribute to amyloid aggregation and neurotoxicity. Methods aimed at specifically reducing levels of these modified peptides, such as by administering antibodies that specifically bind to $A\beta_{N3(pE)-42}$ or $A\beta_{N11(pE)-42}$ and induce their clearance, would therefore be highly beneficial. One of skill in the art would have an expectation of success in inhibiting aggregation and reducing neurotoxicity (see discussion *supra* in regards to the relationship between amyloid aggregation and amyloid-induced neurotoxicity) with the polyclonal antibodies taught by Saido because Schenk teaches that similar polyclonal antibodies (raised against Aβ1-42) administered to PDAPP mice were very effective in significantly reducing amyloid burden in the brains of these animals. Accordingly, because brain amyloid plaques contain the truncated $A\beta_{N3(pE)-42}$ peptide species at noteworthy levels,

the administration of antibodies directed against these peptides would also be expected to result in significant inhibition of amyloid aggregation and clearance of amyloid deposits, thereby reducing Aβ-associated neurotoxicity.

Conclusion

All claims are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kimberly Ballard, PhD
Art Unit 1649
February 23, 2006

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER